PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference N.88273A - GWM	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/001650	International filing date *(day/month/year)* 15.04.2004	Priority date *(day/month/year)* 15.04.2003
International Patent Classification (IPC) or national classification and IPC A61K9/19, A61K38/00, A61K9/48, A61K47/10, A61K47/14		
Applicant AXCESS LIMITED et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☒	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15.02.2005	08.03.2005
Name and mailing address of the International preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Luangkhot, N Telephone No. +49 89 2399-7857

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/001650

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-15 as originally filed

   Claims, Numbers

   1-29 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 28-29 regarding industrial application

because:

☒ the said international application, or the said claims Nos. 28-29 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/001650

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-29
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-29
Industrial applicability (IA)	Yes:	Claims	1-27
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

Basis of the report

1) The use of the terms "its derivatives" or "its analogues" is unclear and contravenes Art.6 PCT because these terms lack explicit boundaries and the scope thereof needs interpretation.
It could mean salts, or chemically similar derivatives such as benzalkonium chloride, benzyl alcohol, salicylate, parabens, phenol derivatives (etc...) , but could also include all compounds having the same mode of action, independently from the chemical structure (glycyrrhizinate). Since a patent claim defines a scope, it is necessary that the boundaries of said scope are well defined in order to guarantee legal certainty. Therefore these terms should be deleted.

Failure to do so lead to novelty objection (see underneath).

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2) Claims 28-29. relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3) The documents cited in the International Search Report (ISR) were numbered respectively from D1-D11; this numbering results from the citation order in the ISR and will be used for the procedure. Unless not specified, the cited passages of each document in the ISR will be considered.

4) The subject-matter of claim 1 and its dependent claims is not novel and/or not inventive because D2 (see claims 1,5,6,8,9,10,17), D3 (see 413-416), D5 (see col.11 L.30-67, claims 1-2,19, example 1, col.2 L.5), D7 (see p.1 L.4-6, p.2 L.12-p.3 L.24, Table 4), D8 (see col.1 L.29-col.2 L.46, claim 5), D9 (Examples 2,4), D10

(see abstract), D11 (see abstract) describe a composition containing:
a/ an active macromolecular principle,
b/ an aromatic alcohol absorption enhancer which can be BHT, BHA or **a derivative or an analogue thereof (such as benzyl alcohol, a salicylate, benzaknium chloride, a parabens,...)**,
wherein the aromatic alcohol absorption enhancer is present in an amount by weight greater or equal to that of the active macromolecular principle.

5) The subject-matter of claim 2 and its dependent claims is not novel and/or not inventive because D2 (see claims 1,5,6,8,9,10,15,17,21, p.2 L.25, p.9 L.24-p.10 L.20), D3 (see 413-416), D5 (see col.11 L.30-67, claims 1-2,19, example 1, col.2 L.5), D7 (see p.1 L.4-6, p.2 L.12-p.3 L.24, Table 4), D8 (see col.1 L.29-col.2 L.46, claim 5), D9 (Examples 2,4), D10 (see abstract), D11 (see abstract) describe a composition containing:
a/ an active macromolecular principle,
b/ an aromatic alcohol absorption enhancer which can be BHT, BHA, propyl gallate or **a derivative or an analogue thereof (such as benzyl alcohol, a salicylate, benzaknium chloride, a parabens,...)**,
c/ a solubilizer capable of increasing the solubility of the aromatic alcohol absorption enhancer in aqueous media,
wherein the aromatic alcohol absorption enhancer is present in an amount by weight greater or equal to that of the active macromolecular principle.

6) The subject-matter of claims 17 and 19 and its dependent claims is not novel and/or not inventive because D2 (see claims 15,17,21), D3 (see 413-416), D4 (see abstract, Table 1), D5 (see col.11 L.30-67, claims 1-2,19, example 1, **col.2 L.5**), D6 (see PAJ abstract), D7 (see p.1 L.4-6, p.2 L.12-p.3 L.24, Table 4) describe the use of BHT, BHA or **a derivative or an analogue thereof (such as benzyl alcohol, a salicylate, benzaknium chloride, a parabens,...)**, as enhancer for the absorption of a macromolecule across the intestinal wall.

7) The subject-matter of claims 18 and 20 and its dependent claims is not novel and/or not inventive because D1 describes the use of BHT or BHA as permeation enhancers in order to enhance the absorption of macromolecular compounds such as DNA or anthracyclines (see §54-57), D2, D3 (see 413-416), D4 (see abstract, Table 1), D5 (see col.11 L.30-67, claims 1-2,19, example 1, **col.2 L.5**),

D6 (see PAJ abstract), D7 (see p.1 L.4-6, p.2 L.12-p.3 L.24, Table 4), D8 (see col.1 L.29-col.2 L.46, claim 5), D9 (Examples 2,4), D10 (see abstract), D11 (see abstract) describe the use of BHT, BHA or **a derivative or an analogue thereof (such as benzyl alcohol, a salicylate, benzaknium chloride, a parabens,...)**, as enhancer for the absorption of a macromolecule.

8) Should the applicant renders the subject-matter of the present application novel by stressing out the relevance a technical feature that is not described explicitly in prior art or by introducing into the claims the use of a **specific compound or a specific ratio** or whatever, inventive step would be recognized **only if he demonstrates** that **a surprising or synergetic effect** is attributed to the introduced technical feature that the skilled man in the art could not deduct from the prior art.

In the absence of a surprising effect in comparison with prior art, inventive step cannot be acknowledged because the introduced technical feature would be considered as an **obvious alternative** that the skilled man in the art would perform **routinely** in order not to interact with prior art.

9) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application.

10) The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). Preferably these indications should be submitted in handwritten form on a copy of the relevant parts of the application as filed.

11) The applicant is kindly requested to take account of the above objections and give

convincing argumentations. Should the applicant regard some particular matter as patentable, an independent claim should be filed taking account of Rule 6.3(b) (I), (ii) PCT (two part form claim). The applicant should also indicate in the letter of reply the difference of the subject-matter of the new claim vis-à-vis the state of the art and the significance thereof.

Re Item VII
Certain defects in the international application

12) For the assessment of the present claims 28-29 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

13) Claims 18 and 20 are formulated as a second medical use claim but do not describe any therapeutical indication. Therefore they **are not admissible in this form** and a rewording would lead to the subject-matter of claims 17 and 9.

14) If present application contains registered trademarks (see for example "Transcutol" in claims 12 and 22), they should be acknowledged as such.

15) Contrary to the requirements of Rule 5.1(a)(ii) PCT, it seems that the relevant background art disclosed in the documents D2-D3 is not mentioned in the description, nor are these documents identified therein.

Re Item VIII
Certain observations on the international application

16) Use of terms such as "derivatives or analogues): see above §1)